

REMARKS

There are 54 claims in the application. Claims 27-40 and 50-54 have been withdrawn. Claims 1-26 and 41-49 are pending. Claims 1-26 and 41-49 have been rejected by the Examiner. Applicants traverse. Claims 11 and 20-23 are hereby canceled without prejudice. Claims 1-3, 12-15, 25, 26 and 45-49 have been amended herein. Support for these amendments can be found throughout the Specification and Claims; however, Applicants direct the Examiner's attention to the Claims as originally filed to find specific support for these amendments. No new matter has been added.

Rejections under 35 U.S.C § 112, first paragraph

Claims 4, 12-15, 25, 26, 45, 46, and 48 and have been rejected under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter that was not described in the Specification in such a way as to convey to one skilled in the art that the inventors were in possession of the invention as claimed. Applicants traverse each and every rejection.

In reference to claims 12 and 41 and the term "derivatives", the Examiner specifically recites the term "derivatives" as not being supported by the Specification. Applicants believe the term "derivatives" would be understood by one skilled in the art. This is especially true of claim 41. Claim 41 further limits claim 4 which excludes the use of "alkaline and/or water-swellaable substances". At the time of filing the Application, Applicants were aware that the use of derivatives of alkaline and/or water-swellaable substances was detrimental to the practice of the invention in that they alter the sustained release characteristics of the claimed formulations. Applicants disclose alkaline and/or water-swellaable substances interfere with the function of the diffusion matrix, *see* pages 17-18 of the Specification. Derivatives of alkaline and/or water-swellaable substances are known and recognizable to one skilled in the art. It is not necessary to list all possible derivatives to advise the skilled artisan to avoid using such compounds when practicing the invention. Applicants submit claim 41 is in compliance with 35 U.S.C § 112, first paragraph. Applicants submit that claim 41 has a clear meaning to one skilled in the art in the context of this application and would be convincing to one skilled in the art that the Applicants were in possession of the invention at the time of application. Amended claim 12 does not recite the term "derivatives" and is therefore believed to be in compliance with 35 U.S.C § 112, first paragraph.

In reference to claims 4 and 41 and the phrase "relevant amount", the Examiner specifically recites the phrase "relevant amount" as not being supported by the Specification.

Applicants believe the term “relevant amount” would be understood by one skilled in the art in the context of the present invention. In the Specification, Applicants disclose alkaline and/or water-swellaible substances interfere with the function of the diffusion matrix, *see* pages 17-18 of the Specification. Significant amounts of such compounds can alter the sustained release characteristics of the claimed formulations. However, trace amounts may not alter the sustained release characteristics of the claimed formulations. The term “relevant amount” would be understood by one skilled in the art to mean an amount that would alter sustained release characteristics of the claimed formulations and would be convincing to one skilled in the art that the Applicant was in possession of the invention at the time of application. Applicants believe that claims 4 and 41 are in compliance with 35 U.S.C. § 112, first paragraph.

Regarding claims 13-15, 25, 26, 45, 46, and 48 and the term “about”, the Examiner specifically recites the term “about” when used in reference to an endpoint of a range as not being supported by the Specification. Applicants have amended these claims to remove the term “about” without prejudice. Applicants believe that claims 13-15, 25, 26, 45, 46, and 48 in compliance with 35 U.S.C. § 112, first paragraph.

Claim 49 was not rejected under 35 U.S.C. § 112, however, it depends on claim 14. If the term “about” remained in claim 49 it would claim material not claimed in the parent claim. Claim 49 has been amended to only claim material also claimed in the parent claim.

Regarding claim 10 and the phrase “admission guidelines”, Applicants have removed the phrase “admission guidelines” from amended claim 10. Applicants believe that claim 10 is in compliance with 35 U.S.C. § 112, first paragraph.

Applicants believe that the above amendments and remarks resolve the Examiner’s concerns regarding enablement. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 112, first paragraph of the pending claims.

Rejections under 35 U.S.C. § 103

Claims 1-26 and 40-49 have been rejected under 35 U.S.C. § 103(a) as being alleged to be unpatentable over EP 0699436 patent to Miller et al. (hereinafter, “the ‘436 patent”) in view of US Patent No. 7,332,182 to Sackler et al. (hereinafter, “the ‘182 patent”) and US Patent 6,306,438 to Oshlack et al. (hereinafter, “the ‘438 patent”). Applicants traverse each and every rejection.

A finding of obviousness under 35 U.S.C. §103 requires a determination of: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the difference between the claimed subject matter and the prior art, and (4) whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1, 17 (1966). Therefore, obviousness inquiries require determining whether the prior art suggests the claimed invention and whether that prior art would have indicated a reasonable expectation of success to one of ordinary skill in the art. *In re O'Farrell*, 853 F.2d 894, 902903, 7 USPQ2d 1673, 1680-1681 (Fed. Cir. 1988). Furthermore, "the prior art must teach or suggest all of the claim limitations." MPEP §§ 2142, 2143, emphasis added.

The Examiner has the burden of establishing a *prima facie* case of obviousness by proving three elements: (1) a particular reference (or combined references) must suggest or teach all the limitations of the challenged claim, (2) a suggestion or motivation from the prior art to modify or combine the reference teachings, and (3) a reasonable expectation of success must exist from the prior art. MPEP §§2142, 2143, citing *In re Vaack*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Care must be exercised not to use the applicant's disclosure to fill in the gaps of the prior art. *In re Vaack*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Applicants respectfully submit that the '438 patent fails to render the claims 1-10, 12-19, 25, 26, and 40-49 obvious. The '438 patent is substantially directed to the disclosure of a diffusion matrix that is composed of swellable and/or alkaline substances. From page 4 of the '438 patent:

Suitable materials for inclusion in a controlled release matrix include

(a) Hydrophilic or hydrophobic polymers, such as gums, cellulose ethers, acrylic resins and protein derived materials. Of these polymers, the cellulose ethers, especially alkylcelluloses are preferred.

In contrast the present invention claims the use of the ethyl cellulose-polymers to produce a substantially non-swellable diffusion matrix. From page 18 of the Specification of the instant application:

Currently, alkylcelluloses will generally also not be considered for the production of formulations in accordance with the invention. Propylcellulose e.g. is of too lipophilic character to produce matrices with release characteristics in accordance with the invention. Methylcellulose is also not suitable for the formulations in accordance with the invention. [Emphasis added.]

Example 1 from the '438 patent, which was cited by the Examiner as possessing much of the elements of the claimed invention contain compounds that are explicitly disclosed as being considered not usable with the invention.

Example 1

Tablets having the following formulation were prepared:

	mg/tablet
Tramadol Hydrochloride	100
Lactose Ph. Eur.	68.0
Ethylcellulose (Surelease®25% solids)	15
Purified Water Ph. Eur.	13.3*
Cetostearyl Alcohol Ph. Eur. (Dehydag wax 0)	42
Magnesium Stearate Ph. Eur.	2.00
Purified Talc Ph. Eur.	3.00
	230.00

* Removed during processing.

Tramadol hydrochloride (100mg) and lactose (68mg) were granulated, transferred to a fluid bed granulator and sprayed with ethylcellulose (15mg) and water. The granules were then dried at 60° C and passed through a 1mm screen.

To the warmed tramadol containing granules was added molten cetostearyl alcohol (42mg) and the whole was mixed thoroughly. The granules were allowed to cool and sieved through a 1.6mm screen. Purified talc and magnesium stearate were added and mixed with the granules. The granules were then compressed into tablets.

The tablets were coated with a film coat having the formulation given below.

	mg/tablet
<u>Hydropropylmethylcellulose</u> Ph. Eur. 15 cps (Methocel E15)	0.770
<u>Hydroxypropylmethylcellulose</u> (Ph. Eur. 5 cps (Methocel E5)	3.87
Opaspray M-1-7111B (33% solids)	2.57
Polyethylene glycol 400 USNF	0.520
Purified Talc Ph. Eur.	0.270
Purified Water Ph. Eur.	55.52*

* Remove during processing. [Emphasis added.]

The tablets of Example 1 of the '438 patent contains hydropropylmethylcellulose. In contrast, the Specification of the instant application discloses that formulations that contain hydropropylmethylcellulose (HPMC) are not usable with the invention. From Page 8 of the Specification:

The aforementioned pain-relief medicament Valoron® is a tilidine/naloxone-combination. According to the manufacturer's data it is a formulation from which both active compounds are released in a sustained manner. The matrix used comprises a relevant part of water-swellaable material hydroxypropylmethylcellulose (HPMC)) and has therefore to be considered as a swellaable (and possibly partially erosive) diffusion matrix. The disadvantage of this known formulation is that tilidine and naloxone, given identical mass ratios but different absolute amounts, display different release profiles, if the release is measured for certain pH values. [Emphasis Added.]

Furthermore on page 18 of the Specification of the instant application, the Applicants further disclose how certain materials are not usable with the invention:

Matrices which are based on polymethacrylates (as e.g. Eudragit® RS30D and Eudragit.RTM. RL30D) or comprise relevant amounts of water-swellaable material, particularly of hydroxyalkylcellulose such as HPMC will currently not be considered usable in accordance with the invention. [Emphasis added.]

One limitation of the claimed invention is a substantially non-swellaable diffusion matrix: the '438 patent alone does not teach each and every claim limitation. Neither the

'436 patent nor the '182 patent by themselves or in combination cure the deficits of the '438 patent. Applicants respectfully submit that in view of the amendments to the pending claims of its application and the remarks above, the Examiner's rejection under 35 U.S.C. § 103 has been overcome, and should be withdrawn.

Double patenting

Claims 1-26 and 40-49 of the instant application stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-44 of copending Application No. 10/510,674. Claims 11, and 20-24 have been canceled. Claims 2-10, 12-19, 25, 26, and 40-49 depend on amended claim 1. Since neither the amended claim 1 nor the claims of copending Application No. 10/510,674 have been patented, Applicants respectfully request that the Examiner withdraw this provisional obviousness-type double patenting rejection until such time when these claims are in final form and otherwise in condition for allowance, and the claims of Application No. 10/510,674 over which double patenting is alleged are allowed. Until such time, there is no double patenting and no way to determine double patenting. MPEP § 804.01.I(B)(1).


Conclusion

It is respectfully requested that the above amendments and remarks be entered into the file of the application. No fee beyond that for the Petition for Extension of Time is believed to be required for the filing of this response. However, the Commissioner is hereby authorized to charge any required fees to Duane Morris LLP Deposit Account No. 04-1679.


Applicants believe that these amendments and remarks place the instant application in condition for allowance and respectfully request and notice of allowance to be issued at this time. However, the Examiner is invited to call the undersigned attorney at (212) 692-1086 if a telephone call could help to resolve these, or any other issue.

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Respectfully submitted,


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Enclosures